DETERMINANTS OF THE DECLINE IN DIOXINS BETWEEN BLOOD DRAWS AMONG WORKER WITH 2,4,5-TRICHLOROPHENOL AND PENTACHLROPHENOL EXPOSURES

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Introduction

Epidemiology studies often use statistical models to predict historical occupational exposure levels of 2,3,7,8 tetrachlorodibenzo-p-dioxin (TCDD) from current serum measurements. The validity of such models depends in part on an accurate determination of the rate at which dioxins are cleared from the body, as well as on certain other physiological factors.

Concentrations of TCDD above background levels have been measured in the serum of 2,4,5-Trichlorophenol (TCP) workers and elevated concentrations of higher chlorinated dioxins in pentachlorophenol (PCP)workers.[1] We have used serum measurements to estimate past occupational exposures to TCDD and to higher chlorinated dioxins,) including 1,2,3,4,7,8 hexachlorodibenzo-p-dioxin (1,4 HXDD), 1,2,3,6,7,8 hexachlorodibenzo-p-dioxin (1,6 HXDD), 1,2,3,7,8,9 hexachlorodibenzo-p-dioxin (1,9 HXDD), 1,2,3,4,7,8,9 heptachlorodibenzo-p-dioxin (HPDD), and octachlorodibenzo-p-dioxin (OCDD). Mortality risks among chlorophenol workers from dioxin exposures estimated in this way have been recently reported.[2, 3]

The current study re-sampled a subset of chlorophenol workers to examine the elimination rates of dioxins and to identify other determinants of serum dioxin concentrations. Some investigations have reported a wide range of half-lives for some dioxins; for TCDD, values in adults from 6.1 to 11.3 years can be found.[4-6] Less information is available on the half-lives of higher chlorinated dioxins found in PCP operations, although estimates from 4 to 16 years have been reported.[7] In addition, factors such as chloracne, age, amount of body fat, and smoking have been related to dioxin levels or elimination rates.[4-6] Thus, a chlorophenol worker's current serum levels are influenced by duration and intensity of past exposures and elimination rates, as well as the factors related to both.

Table 1. Sampling scheme and participation rates in 2010 serum study.

Serum concentration from previous study	***Sampling fraction***	***Workers under age 80***	***Participants****	***Participation Rate***
TCDD				
High (>50 ppt)	1.0	12	7	58%
Medium (10-50 ppt)	0.5	89	28	63%
Within Background (<10 ppt)	0.15	205	21	68%
Total		306	56	64%
OCDD				
High (>5000 ppt)	1.0	9	6	67%
Medium (1000-5000 ppt)	0.5	69	26	75%
Within Background (<1000 ppt)	0.15	228	24	70%
Total		306	56	72%

*9 workers had high serum concentrations of both TCDD and OCDD, consistent with job exposures in both TCP and PCP operations.

Materials and Methods

Candidates for the present serum dioxin study had been sampled in the previous blood draw conducted in 2004 or 2005 and were less than 80 years old in 2010. Serum TCDD level in 2004 or 2005 was used as an indicator of past TCP exposure, and serum OCDD as an indicator of PCP exposure. Because above-background levels of TCDD and OCDD are more informative, we sampled more heavily among the workers with the highest levels of dioxins from the previous study. Serum categories for sampling were chosen to approximately represent background, the medium range (1 to 5 times the background range), and the highest range (greater than 5 times the background range) of values from 2004-5, as shown in Table 1.[8] We invited all subjects in the highest range, half the subjects in the medium range and 15% of the workers in the lowest category to participate. Actual participation rates for each category are shown in the final column of Table 1. Some workers who held jobs in both TCP and PCP operations had both high TCDD and high OCDD levels. Overall, 56 chlorophenol workers (72% of those eligible) participated in the study.

Table 2. Multiple regression parameter estimates and standard errors (SE) for selected predictors of dioxin congener serum values.

Variable	2,3,7,8-TCDD (SE)	OCDD (SE)	TEQ (SE)
Percentage Change in Serum Concentration 2004-2010			
Intercept	-0.6 (0.8)	-0.1 (0.5)	-0.4 (0.3)
Days since draw	0.1 (0.1)	0.1 (0.0)*	0.1 (0.0)*
Age	0.0 (0.1)	-0.0 (0.0)	0.0 (0.0)
Body Mass Index	0.0 (0.0)	0.0 (0.0)	0.0 (0.0)
Chloracne	-0.0 (0.1)	0.0 (0.0)	-0.0 (0.0)
R^2	0.08	0.20	0.21
P-value	0.380	0.020	0.018
Absolute Change in Serum Concentration 2004-2010			
Intercept	38.7 (23.9)	-81.9 (273)	56.3 (27.0)*
Days since draw	2.5 (2.5)	-483 (287)	-1.1 (2.8)
Age	-0.7 (0.2)*	38.3 (22.1)	-0.9 (0.2)*
Body Mass Index	-0.5 (0.3)	-31.7 (34.3)	-0.6(0.3)
Chloracne	5.3 (1.9)*	415 (219)	9.6 (2.2)*
R^2	0.31	0.34	0.50
P-value	0.001	0.000	0.000
Serum Concentration in 2004-5			
Intercept	-156 (49.4)	2902 (3355)	-142 (53.9)
Age	1.8 (0.5)*	-32.6 (35.8)	2.3 (0.6)*
Body Mass Index	1.8 (0.9)*	55.9 (60.4)	2.1 (1.0)*
Chloracne	-7.0 (4.2)	-1142 (288)*	-18.2 (4.6)*
R^2	0.25	0.31	0.41
P-value	0.002	0.000	0.000
Serum Concentration in 2010			
Intercept	-79.1(32.7)	374(2059)	-56.7(42.5)
Age	1.0 (0.4)*	8.6(22.9)	1.3(0.5)
Body Mass Index	0.7 (0.6)	12.7(35.6)	0.6(0.7)
Chloracne	-3.7 (2.9)	-534(182)*	-9.6(3.8)*
R^2	0.17	0.16	0.21
p-value	0.023	0.030	0.006

*significant at 0.05.

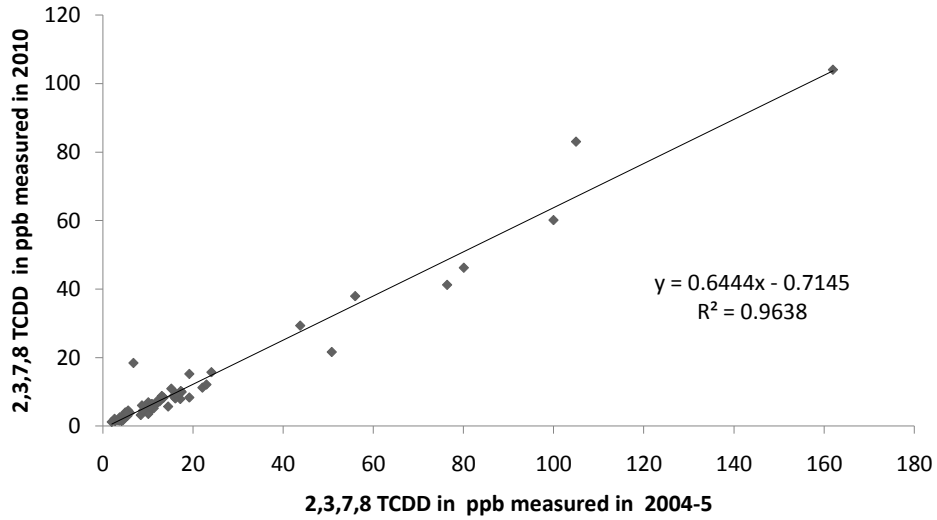
We conducted and analyzed the serum in 2010 using the same protocol, procedures and laboratory as in the 2004-5 blood draw. Serum samples were tested for 7 dioxins, 10 furans and 15 PCBs, but since previous studies on these workers indicated that workplace exposures increased only dioxins levels, we address only dioxins in this investigation. However, we did calculate the toxic equivalent (TEQ), a weighted sum of measured dioxin, furan, and PCB values. Study conduct was reviewed and overseen by a Human Subjects Review Board in Midland, Michigan. All study subjects participated voluntarily and signed a consent form.

In examining the determinants of serum concentrations and elimination rates, we modeled a) the percent decline and b) the absolute decline in serum concentrations between 2004-5 and 2010, as well as c) the specific serum concentrations in 2004-5 and d) in 2010. The potential determinants we examined included age, a measure of amount of body fat (body mass index, BMI), change in BMI between the 2 samples, current cigarette smoking, and whether the worker developed chloracne while exposed. The criteria for chloracne diagnosis was defined in a previous study.[9] In comparing the 2 blood draws, we included the time between the draws as a factor.

Results and Discussion

Figure 1 plots the serum TCDD levels for 56 workers from the blood collections in 2004 or 2005 with the same workers serum TCDD levels in 2010. With the exception of one worker, the TCDD levels decreased for every worker. The average decrease for all workers between the two blood draws was 39% for TCDD. The R squared for TCDD was 0.96. While not shown, the decrease for the other dioxin congeners, the furans and the PCBs displayed similar decreases and there was a strong correlation between the dioxin levels in 2004-5 and 2010.

Table 2 presents multiple regression results for the percentage change and the absolute changes in serum levels, and on the 2004-5 and 2010 serum levels of TCDD, OCDD and the TEQ. We did not find current cigarette smoking or change in body fat between samples predictive in any of the models for any of the dioxins, so these factors are not presented. For the percentage change between 2004-5 and 2010, there are no significant predictors other than days since the blood draw for OCDD and the TEQ. For the absolute change, age and past chloracne are significant predictors for TCDD and the TEQ. In the 2004-5 blood draw, age and body mass index are significant predictors for TCDD and the TEQ and previous chloracne is a predictor also for the TEQ and OCDD. For the 2010 blood draw, age is a significant predictor for TCDD, and past chloracne is a significant predictor for OCDD and the TEQ.



For most of the chlorophenol workers studied, we found a decrease in dioxin levels and a strong association between dioxin levels from sampling in 2004-5 and 2010. The amount of decline in the dioxin levels is consistent with several previous studies. Age, body mass index, and previous case of chloracne were important determinants of dioxin levels measured in both time periods and the level change between periods again consistent with previous studies. However, none of these factors were related to percentage change. The absence of any association between percentage change in elimination and age and body mass index is in contrast with a previous study of chlorophenol workers done by Flesch-Janys et al.[7] That study found age, percentage of body fat, and hepatopathia were associated with TCDD elimination rate and percent body fat and smoking status with OCDD elimination rate. The lack of such associations in our study may be because a) our study had lower average dioxin levels in both time periods, b) our study population is older and c) likely has a narrower age and body mass index range.

We found previous diagnosis of chloracne was an important predictor of current serum dioxin levels. Most of the cases of chloracne occurred 40 to 50 years ago and are still important for understanding current dioxin levels among these chlorophenol workers. The development of chloracne in our study is related to higher dioxin exposures. Chlorophenol workers with a diagnosis of chloracne from TCP, PCP, or both have dioxin exposure levels higher than workers who are not diagnosed with chloracne but had chlorophenol exposure. Chlorophenol workers who were only exposed to TCP had elevated levels of TCDD while the workers only exposed to PCP had elevated levels of the higher chlorinated dioxins including the 3 HxCDDs, the HpCDD and the OCDD. These findings are consistent with several other studies of TCP and PCP workers.

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